

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Does more education mean less disability in people with dementia? A large cross-sectional study in Taiwan
<b>AUTHORS</b>	Huang, ShihWei; Chi, Wen-Chou; Yen, Chia-Feng; Chang, Kwang-Hwa; Liao, Hua-Fang; Escorpizo, Reuben; Chang, Feng-Hang; Liou, Tsan-Hon

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Ove Almkvist Department of Neurobiology Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden
<b>REVIEW RETURNED</b>	29-Sep-2016

<b>GENERAL COMMENTS</b>	<p>The study investigates the relationship between cognitive reserve categorized as with and without formal education versus disability status evaluated by WHODAS (four degrees of disability in six domains) in 7698 demented Taiwanese individuals 65 years or older. Results showed a significant positive relationship in two domains ("getting along" and "social participation") but not in the other four domains ("cognition", "mobility", "self-care", and "life activities").</p> <p>The following points are suggested to be considered by the authors to improve the manuscript. First, the concept of cognitive reserve is commonly treated as a quantitative entity, but in the paper it is a binary entity. This fact is problematic. Maybe the degree of education could be added in order to investigate the dose relationship between cognitive reserve and disability in those individuals who have had a formal education. In those who have not had a formal education it may be possible to quantify the degree of cognitive demands in the life occupation?</p> <p>Second, the collection of data on WHODAS was performed by a number of investigators implying a risk of confounding. Please mention if investigators were comparable in their reports on disability. Furthermore, it is said that some of the demented participants had difficulties to communicate a report on their disability. This factor could be investigated and the result would be</p>
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	<p>important to know. Another point regarding WHODAS is that it is hard for a reader to understand what is meant by the six terms used to present the content of WHODAS. It is necessary explains the six terms.</p> <p>Third, the concept of dementia was evaluated following ICD criteria. What kind of information/data was used to compare with the ICD criteria? Which dementia diseases except Alzheimer's existed in the data base. With a total sample size of 7700 individuals many different diseases should be found, please report, and more importantly, separate the analyses stratified by type of dementia. The different dementia disease may have a differential impact on WODAS! If so, the current results are confounded by dementia type?</p> <p>Fourth, the expected finding that cognitive reserve should be related to the WHODAS domain 1 was not obtained. This is strange since this is a typical finding in previous research. The explanation given for this result is speculative and it is not supported by empirical data. Also, the significant findings on "getting along" and "social participation" are not explained in a satisfactory manner. How are these variables related to education as studied by illiteracy? This has to be dealt with in more detail and supported by data. Maybe the different items in the target concepts may help delineate the patterns of associations?</p> <p>Finally, the conclusions in the abstract as well as in the last section of the discussion are not conclusions but repetition of results. Please try to describe implications of the results.</p> <p>It is suggested that the manuscript is revised before a final decision is possible regarding publication or not.</p>
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<b>REVIEWER</b>	Catherine Dotchin Northumbria Healthcare NHS foundation trust UK
<b>REVIEW RETURNED</b>	04-Oct-2016

<b>GENERAL COMMENTS</b>	This paper outlines the disability level for patients with dementia enrolled on a Taiwanese national database as defined by the WHODAS 2. Comparison is made between those with and without formal schooling. The authors report that in those with no formal education scores in all domains of the WHaoDS were associated with education, apart from self care. It would be helpful if the authors
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	<p>could expand on how patients are enrolled into this database. Are all of those seen by a doctor and diagnosed automatically registered, or do patients have to apply? Also, is it likely that all people with dementia will be on this registry? Could those with lower schooling and lower socioeconomic status not be included?</p> <p>In the abstract the authors refer to 3846 patients in each group but in the main section 3849 in each group. Please correct. There are a couple of typos - in the abstract lower not low disability status, and bottom of page 12 "stark" contrast, not start. On page 14 the authors state that most older people in Taiwan lack formal schooling, yet in this study the numbers were half and half schooling and non schooling. Is this therefore a representative sample? Please clarify who decided whether a patient or carer gave the who das answers.</p>
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## VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Ove Almkvist

Institution and Country: Department of Neurobiology Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden

Review regarding bmjopen-2016-013841 The study investigates the relationship between cognitive reserve categorized as with and without formal education versus disability status evaluated by WHODAS (four degrees of disability in six domains) in 7698 demented Taiwanese individuals 65 years or older. Results showed a significant positive relationship in two domains ("getting along" and "social participation") but not in the other four domains ("cognition", "mobility", "self-care", and "life activities"). The following points are suggested to be considered by the authors to improve the manuscript.

First, the concept of cognitive reserve is commonly treated as a quantitative entity, but in the paper it is a binary entity. This fact is problematic. Maybe the degree of education could be added in order to investigate the dose relationship between cognitive reserve and disability in those individuals who have had a formal education. In those who have not had a formal education it may be possible to quantify the degree of cognitive demands in the life occupation?

Response:

Thank you for this. With concerning the demographic confounding effects, we used the propensity score matching and simplified as with formal education and without formal education groups. As your precious suggestion, we further analyzed the degree of formal education among with formal education group and revised related part (We separated the formal education group as Basic education (elementary school+junior high school and senior high school+college school or above)). And the further analyzed result as follows:

Overall disability (based on WHODAS II scores) in different domains between elderly Taiwanese dementia patients with( Literacy Group) formal education (N = 3,849)

Basic Education(Elementary+Junior)n=3,149 Advance Education(Senior + college(or above))n=700

Mean SD Mean SD P value

Domain 1 71.72 27.179 72.21 26.569 0.669

Domain 2 57.37 33.690 60.38 33.027 0.032\*

Domain 3 43.25 35.960 46.27 36.124 0.045\*

Domain 4 71.82 29.599 73.69 28.689 0.128

Domain 5 79.07 32.393 81.13 32.603 0.129

Domain 6 51.06 26.664 52.87 26.634 0.103

Summary 61.52 24.086 63.42 23.866 0.059

Our data presented high WHODAS 2.0 disability scores of the domain 2 and domain 3 for higher educated dementia patients. It may indicated that higher education disabled dementia patients had more disability of mobility and self care. But the demographic data were not controlled between basic education and advanced education group. When we further analyzed these two groups with PS matching method, there was no statistical significant difference of all the domains of WHODAS 2.0. However, for consistence of non-education group and simplified the influence of education, we didn't added this information in this revised version.

Unfortunately, the cognitive demands in life and occupation cannot be obtained of our database. We added this in limitation part as follows" Third, community environment, family support, and marriage status were not controlled for in this study. Besides, the cognitive demands in life and occupation cannot be obtained of our database. Nevertheless, we controlled for the urbanization level, residence status, and socioeconomic status, and these variables can represent the living environment and social resource of the disabled dementia patients for minimizing these confounding factors."

(Page 16 Line 13~28)

Second, the collection of data on WHODAS was performed by a number of investigators implying a risk of confounding. Please mention if investigators were comparable in their reports on disability. Furthermore, it is said that some of the demented participants had difficulties to communicate a report on their disability. This factor could be investigated and the result would be important to know. Another point regarding WHODAS is that it is hard for a reader to understand what is meant by the six terms used to present the content of WHODAS. It is necessary explains the six terms.

Response:

Thank you for this. We bias caused by different investigator and proxies were inevitable in this nation wide database analysis. Hence we stated it in the limitation part as follows" the WHODAS 2.0 assessment was performed on the basis of the responses given by dementia patients or their caregivers, which might have underestimated the functioning disability for dementia patients with mild severity of disability and poor insights. Most dementia patients with extreme severity had limited ability to communicate with the interviewer and thus could not respond to the questionnaires; therefore, their assessment was completed by proxies".

(Page 15 line 39~54)

The evaluation accuracy was mentioned at the end of outcome measure part as follows "The traditional Chinese version of WHODAS 2.0 is used in TDPD database; the intraclass correlation coefficient of this version of the questionnaire was found to be 0.80–0.89, and the internal consistency and reliability was found to be 0.73–0.99 (Cronbach's  $\alpha$ )"

(Page 10 line 27~36)

With concerning the WHODAS, we will add more information can explain the six terms in introduction part as follows " The WHO (World Health Organization) Disability Action Plan was proposed to strengthen the collection of data on disability assessment and further identifying needs when planning healthcare services, and allocating medical resources during 2014 to 2021. In 2001, the International Classification of Functioning, Disability, and Health (ICF) was developed to comprehensive evaluation impairments, activity limitations, participation restrictions, personal and environmental factors. Based on the ICF concept, the WHO developed an assessment tool named WHO Disability Assessment Schedule (WHODAS) and 2.0 Version (WHODAS 2.0) was published in 2010."

(Page 6 line 6~30)

Third, the concept of dementia was evaluated following ICD criteria. What kind of information/data was used to compare with the ICD criteria? Which dementia diseases except Alzheimer's existed in the data base. With a total sample size of 7700 individuals many different diseases should be found, please report, and more importantly, separate the analyses stratified by type of dementia. The different dementia disease may have a differential impact on WODAS! If so, the current results are confounded by dementia type?

Response:

Thank you for mention this. The ICD coding was based the Neurologist and Psychiatrist for disability certification process according clinical diagnosis. In addition to Alzheimer's type of dementia, other types of dementia such as vascular dementia were also enrolled in this database. We will further present different type of dementia by different ICD coding (senile dementia 290, Alzheimer disease 331) with percentage of both groups and revised the table 1.

Fourth, the expected finding that cognitive reserve should be related to the WHODAS domain 1 was not obtained. This is strange since this is a typical finding in previous research. The explanation given for this result is speculative and it is not supported by empirical data. Also, the significant findings on "getting along" and "social participation" are not explained in a satisfactory manner. How are these variables related to education as studied by illiteracy? This has to be dealt with in more detail and supported by data. Maybe the different items in the target concepts may help delineate the patterns of associations?

Response:

Thank you for mention this. For controlling the bias caused by different severity of dementia between both groups, we controlled the percentage of severity of both groups. This process could lead the domain 1 score no different between both groups because the severity of dementia mostly determined by degree of cognitive impairment. We revised this in discussion part as follows "Another possible reason of no cognitive disability influence by education is caused by statistical method. In order to control the bias caused by different severity of dementia between both groups, we matched the percentage of severity of both groups. This process could lead the domain 1 score no different between both groups because the severity of dementia mostly determined by degree of cognitive impairment."

(Page 13 line53~Page 14 line 10)

In the aspect of getting alone people and social participation, we will explain more extensively in discussion part as follows" Although there were statistical less disability score of social participation and getting alone with people in such large sample sized study, there were only 2 points difference of standardized score between these two groups. Formal education experience could lead individuals to learn the items of social participation and getting alone people domains such as joining community activities, dealing with people, maintaining a friendship, etc."

(Page 14 Line 44~page 15 line 4)

Finally, the conclusions in the abstract as well as in the last section of the discussion are not conclusions but repetition of results. Please try to describe implications of the results. It is suggested that the manuscript is revised before a final decision is possible regarding publication or not.

Response:

We revised the conclusion and tried to describe the implication of results as follows" Regarding public health aspects, community intervention of social participation should be implemented for elderly

dementia patients especially those without formal education experience to maintain better social interaction ability. Our study provided the education influence on disability status after the event of dementia diagnosis. Detailed investigation of association between education level and social participation among dementia patients is recommended in the future.”

(Page 17 line 4~line19)

Abstract” For disabled dementia patients without formal education, community intervention of social participation should be implemented to maintain better social interaction ability “

(Page 3 Line 52~line 56)

Reviewer: 2

Reviewer Name: Catherine dotchin

Institution and Country: Northumbria Healthcare NHS foundation trust, UK

This paper outlines the disability level for patients with dementia enrolled on a Taiwanese national database as defined by the WHODAS 2. Comparison is made between those with and without formal schooling. The authors report that in those with no formal education scores in all domains of the WHaods were associated with education, apart from self care.

It would be helpful if the authors could expand on how patients are enrolled into this database. Are all of those seen by a doctor and diagnosed automatically registered, or do patients have to apply? Also, is it likely that all people with dementia will be on this registry? Could those with lower schooling and lower socioeconomic status not be included?

Response:

Thank you for this. We expand the how patients enrolled into this database in material and method part.

All these participants in this database must been diagnosis by a doctor and the process started when they applied the certification. If people didn't applied the disability certification, they were not enrolled in the registration database (Taiwan Data Bank of Persons with Disability)

All the disabled people had the rights to apply the disability certification and applied the social welfare support. Especially for low social economic status patients, the social workers of our government would pay more attention to them and provide the supportive resources. Therefore, I think the lower social economic and lower schooling patients had the same opportunity of included in this study.

We added in material and method part as” All the disabled people have the rights to apply the disability certification and they initiated the DES-2012 evaluation process”.

“After the DES-2012 process completed, the data of each applied disabled patients were registered in the TDPD database.”

(Page 7 Line 33~39)

In the abstract the authors refer to 3846 patients in each group but in the main section 3849 in each group. Please correct. There are a couple of typos - in the abstract lower not low disability status, and bottom of page 12 "stark" contrast, not start. On page 14 the authors state that most older people in Taiwan lack formal schooling, yet in this study the numbers were half and half schooling and non schooling. Is this therefore a representative sample? Please clarify who decided whether a patient or carer gave the who das answers.

Response:

Thank you for pointing this out. We corrected this error

(Page 3 Line 26)

This is a represented sample. And we matched the demographic data of them by statistic method (propensity score matching). Therefore our study presented half schooling and half non schooling of the participants.

The interviewers determined the WHODAS 2.0 answered by caregiver or patients and we presented in material and method part as follows” The scores are assigned by authorized specialists after they interview the patients (or their proxies if patients are unable to answer the WHODAS 2.0 questionnaire).”

(Page 9 Line 39~45)

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Fan Wang Cleveland Clinics Foundation United States
<b>REVIEW RETURNED</b>	17-Feb-2017

<b>GENERAL COMMENTS</b>	<p>Overall, data analysis is appropriate, I have several comments that are helpful to improve this manuscript:</p> <ol style="list-style-type: none"><li>1. In Table 1, demographic variants are balanced expect dementia type. The authors should clearly describe the inclusion/exclusion criteria of sample recruitment. For example, the total samples from which 7698 samples were selected, exclusion criteria for those samples not analyzed in this study, proportion of samples who used proxies for questionnaires.</li><li>2. Dementia type is not balanced between 2 groups, the authors need explain why it was not included in regression analysis (Table 3).</li><li>3. Poisson regression model was used to analyze associations of education with WHODAS score, the rational of Poisson regression model should be spelled out, why it is a suitable model given data presented in this study?</li><li>4. In table 3, p values should be listed along with effect sizes. I feel not necessary to present demographic variables, which are supposed to controlled for.</li></ol>
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## VERSION 2 – AUTHOR RESPONSE

Reviewer Name

Fan Wang

Institution and Country

Cleveland Clinics Foundation

United States

Please state any competing interests or state ‘None declared’:

None

Please leave your comments for the authors below

Overall, data analysis is appropriate, I have several comments that are helpful to improve this manuscript:

1. In Table 1, demographic variants are balanced expect dementia type. The authors should clearly describe the inclusion/exclusion criteria of sample recruitment. For example, the total samples from which 7698 samples were selected, exclusion criteria for those samples not analyzed in this study, proportion of samples who used proxies for questionnaires.

Response:

Thank you for this. The control group was obtained by statistic method (propensity score) with 1:1 ratio to study group. Therefore, we didn’t mention the exclusion criteria.

2. Dementia type is not balanced between 2 groups, the authors need explain why it was not included in regression analysis (Table 3).

Response:

Thank you for mention this and we analyzed the regression analysis with types of dementia in this revised version. The table 3 was revised.

3. Poisson regression model was used to analyze associations of education with WHODAS score, the rational of Poisson regression model should be spelled out, why it is a suitable model given data presented in this study?

Response:

Thank you for mention this. We adopt the Poisson regression to identify the association of category variables (demographic data and type of dementia) and the WHODAS 2.0 scores (continuous variables). This was added in statistic part.

4. In table 3, p values should be listed along with effect sizes. I feel not necessary to present demographic variables, which are supposed to be controlled for.

Response:

Thank you for mention this. We added the type of dementia in the regression model. With concerning the demographic data, we considered it still can be analyzed in the regression model even these variables were controlled in control group because we used the Poisson regression analysis to find the association of these categories variables of demographic data, education level, and type of dementia between WHODAS 2.0 scores. Although the demographic variables were not essential controlled of table 3, we still didn't removed these variables because we considered that these data can also be presented to the readers. We calculated the effect size and tried to present it in table 3, but it could lead the table too complicated with detailed p value. Therefore we only presented as previous form with type of dementia.